10

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,340	11/23/1999	Graca Raposo	255/013-US	8331

34313 7590 03/10/2004

ORRICK, HERRINGTON & SUTCLIFFE, LLP
4 PARK PLAZA
SUITE 1600
IRVINE, CA 92614-2558

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,340	RAPOSO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,21 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 5, 7, 21, 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4, 5, 7, 21 and newly added Claim 30 are pending and being acted upon.

2. In view of Applicant's amendment and response, filed 10/27/03, all previous rejections have been withdrawn. In particular, Applicant's amendment and arguments regarding the requirement that the claimed method be capable of actually eliciting a CTL response, a capability not demonstrated in the prior art.

3. The following are new grounds for rejection.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 4, 5, 7, 21 and newly added Claim 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) In Claim 1, it is unclear how a lactadherin and a "polypeptide comprising a lactadherin amino acid sequence" differ. Additionally, it is unclear precisely what the phrase "represented by the RGD motif" means, i.e., how "represented" differs from the commonly used terms "comprising" or "consisting of".

B) In Claim 21, the phrase "comprising of a functional integrin binding site" would more properly be "comprising a functional integrin binding site".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 4, 5, 7, 21 and newly added Claim 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method would elicit and stimulate a CTL immune response.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding a method for eliciting and stimulating a CTL immune response comprising administering lactadherin and a tumor antigen, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the medical art is such that relatively little is known regarding the claimed method of eliciting and stimulating a CTL immune response comprising administering lactadherin and a tumor antigen.

It is noted that given the language of the instant claims the claimed invention is intended to encompass significant breadth. For example, at its most basic, the method requires only the administration of a tumor antigen and an RGD tripeptide capable of binding an integrin. This composition clearly could

not function through the asserted (but not demonstrated) mechanism of binding antigen to dendritic cell (DC) and somehow stimulating an immune response. Said binding would at minimum require an integrin binding site **and** an antigen binding site. Indeed, administration of an RGD integrin-binding site alone would more likely inhibit antigen binding by blocking said sites on DCs (presuming the asserted mechanism is actually functional) and act as an immunosuppressor. Also note the recitation of numerous asserted "tumor antigens" in Claim 30. Said antigens include p53. It is well-known however, that p53 is not a tumor antigen; p53 is actually a tumor suppressor. It is a lack of functional p53 (or the presence of mutated p53) that is thought to induce cancer. Accordingly, the claimed method would not likely provide an effective method for treating cancer. At best, the claimed method would be highly unpredictable and requiring of undue experimentation.

Given such breadth, significant enablement commensurate with the scope of the claims would be required. Said enablement would likely include discussion and disclosure of specific compositions employed in relevant *in vivo* or *in vitro* models demonstrating the functionality of the claimed method.

A review of the specification discloses only vague discussions and no demonstrations of any *in vivo* or *in vitro* efficacy. Indeed, the examples of the specification disclose only that lactadherin is found in a DC cell line and that various mutant lactadherin constructs can be made. Said disclosure is insufficient support for the invention of the instant claims comprising a method of treating cancer by eliciting an immune response.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of physiological activity, the lack of sufficient specific guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 1, 4, 5, 7, 21 and newly added Claim 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of "a lactadherin", as recited in Claim 1. The specification defines lactadherin as "a protein of mammalian origin, expressed at the surface of milk fat globules, and comprising a RGD site and a domain homologous to the factor VIII C-terminal region". The specification fails however, to disclose any "homologous domains" of "the factor VIII C-terminal region". Additionally, the specification discloses that a lactadherin can be human lactadherin and "any functional analogs thereof". Said "analogs" comprise "post-translational modifications" including (but not limited to) deletions, substitutions and additions. No such analogs are disclosed. Given the lack of sufficient disclosure, and the essentially unlimited number of proteins and peptides that might comprise "a lactadherin" by the instant definition, one of skill in the art must conclude that the specification fails to disclose an adequate written description of the claimed invention. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

Please Note: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

3/5/04
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER